On Visceral Sensation and especially that of the Stomach.

Inaugural-Dissertation

zur

Erlangung der Doktorwürde

in der

gesamten Medizin

verfasst und einer

hohen medizinischen Fakultät

der

Kgl. bayer. Ludwig-Maximilians-Universität zu München

vorgelegt von

F. R. Miller.

München 1911.
Kgl. Hofbuchdruckerei Kastner & Callwey.

On Visceral Sensation and especially that of the Stomach.

Inaugural-Dissertation

zur

Erlangung der Doktorwürde

in der

gesamten Medizin

verfasst und einer

hohen medizinischen Fakultät

der

Kgl. bayer. Ludwig-Maximilians-Universität zu München

ACAD.
MED. BAT.
BIBL.

vorgelegt von

F. R. Miller.

München 1911.
Kgl. Hofbuchdruckerei Kastner & Callwey.

Gedruckt mit Genehmigung der medizinischen Fakultät der Universität München.

Referent: Prof. Dr. Otto Frank.

THE sensitivity of the internal viscera has been, in recent years, the subject of considerable speculation and inquiry for, whilst disease of many internal organs is associated with intensely painful impressions, artificial stimulation applied to the normal structures leads to little, if any, effect. Thus, in spite of the acute agony, which is such a familiar symptom in cases of angina pectoris, the observations of Harvey and Ziemssen[1] on the exposed human heart caused them to conclude that the latter is insensitive to stimuli applied to its outer surface.

Although it has frequently been impossible to demonstrate experimentally the sensitivity of the viscera it is a familiar fact that afferent visceral impulses are essential in a large number of normal physiological processes. In micturition and defaecation, for example, impulses from the distended bladder and rectum excite impressions in the brain, but the reflexes may also be carried out, provided only the lumbar portion of the cord is intact.

The explanation of the absence of sensations in response to various forms of artificial stimulation applied to the viscera is, therefore, to be found, not in the insensitivity of the lat-

ter but rather in the fact that the appropriate stimuli have not been applied. Distention of the bladder and rectum or inflammatory processes in many viscera may be regarded as adequate stimuli and these give rise to distinct sensory impressions.

The sensation of pain, although one of the most frequent of all clinical manifestations, cannot be said to afford, in every instance, accurate or valuable indications in regard to the diagnosis of a particular case, for some of the most dangerous diseases, such as cancer of various internal organs, may progress to an advanced stage, without the subject being in the least aware of their existence. On the other hand, the torturing pains of neuralgia appear quite out of proportion to the extent of the lesion or the seriousness of the case. Viewed, therefore, from the teleological standpoint, we do not find, in the case of pain, that degree of precise adaptation which characterises so many biological reactions. Although definite nerve-endings are present in the skin for the perception of pain, touch, and temperature, it is as yet difficult to state which nervous structures are concerned in the appreciation of visceral pain.

It is impossible to underestimate the value of pain in the diagnosis of many internal diseases. Nevertheless, the irregularities and idiosyncrasies in its nature and distribution are familiar clinical facts. The observations

of Head[2] have caused him to conclude that pain arising in a particular viscus is referred to the distribution of the cutaneous sensory nerves, which terminate in the same segment of the cord as do the afferent nerves from the viscus. Thus, in disease of the stomach, pain is referred to the area of skin overlying this organ.

Disease of the various internal viscera is accordingly associated with characteristic are as of cutaneous tenderness and these latter have proved of the utmost service in locating many pathological lesions.

Experiments on animals have afforded valuable contributions to our knowledge of visceral sensitivity, although, in this case, it is frequently difficult to secure evidence regarding the nature of the sensations experienced by the animal. Our deductions regarding visceral sensitivity must, accordingly, depend on the results of observing comparatively simple reactions. In anaesthetised animals the reactions selected have been, in most cases, alterations in the pulse and respirations and vomiting. If, accordingly, we use the term sensitivity in reference to the possibility of exciting, by stimulation of the viscera, various reflex reactions, whether or not these are also accompanied by psychical impressions, then we may expect to obtain, from an experimental study, important evidence regarding visceral sensation.

The earlist experimenter in this direction was Goltz[3], who, in his well-known "Klopfversuch", demonstrated that reflex cardiae inhibition may be produced in frogs by tapping the exposed intestines with the handle of a scalpel. The results obtained by Goltz were extended by Bernstein[4], who showed that the sensory paths concerned were contained in the two sympathetic cords and that they enter the spinal cord between the 3rd and 6th vertebrae, whence they are conveyed to the medulla.

Some experiments were carried out by the writer in the Physiological Institute, München, and, in order to avoidescape of current, tripolar electrodes were used for stimulation. These electrodes were found on trial to offer great advantages over the ordinary ones.

Dec. 23rd 1910.

Stimulation of the stomach with tripolar electrodes (sec. distance 7 cm) causes cardiae inhibition. The oesophagus was then divided and the stimulation of the stomach repeated, but no inhibition was obtained, although the current was increased to its greatest intensity (sec. distance 0 cm).

Dec. 24th 1910.

Stimulation of the sympathetic cords at the point where the two aortae unite causes inhibition (sec. dist. 8 cm).

Dec. 26th 1910.

Stimulation of rectum causes no inhibition (sec. dist. 6—4 cm).

Stimulation of the cardiac portion of the stomach causes, however, inhibition (sec. dist. 6 cm). The oesophagus was then divided and the stimulation repeated but no inhibition resulted.

From the above experiments I am inclined to believe that, in addition to the sympathetic branches to the intestine, the gastric branches of the vagus convey impulses to the medulla which are capable of exciting reflex cardiae inhibition. Further confirmatory experiments on this point are, however, necessary.

The sensory innervation of the peritoneal surfaces of the stomach was the subject of an elaborate research carried out by Ducceschi[5] on doys and cats.

The method of investigation consisted in observing the effect of electrical and mechanical stimulation of the exterior of the stomach on the respirations and general reactions of the animals. Records were taken of the respiratory movements and, since a Verdin's cardiograph was used for this purpose, some of the other reactions of the animals were preserved in the tracings. The occurrence of general agitation, groans, cries and particularly vomiting were also noted and served as valuable indications of sensations excited by gastric

stimulation. Electrical stimulation was applied to the exterior of the stomach and the whole peritoneal suface explored by passing from the pylorus to the cardia, or in a direction opposite to the course of the nerves.

When the extrinsic nerves remain intact stimulation of the stomach causes alterations in the depth and frequency of the respirations of inconstant character. General agitation, groans, wagging of the tail, and vomiting are also observed.

The sensitivity of the pylorus, as indicated by these reactions, is considerably greater than that of the cardia.

After division of the splanchnic nerves the same general reactions, including vomiting, are obtained on stimulation of the stomach. A longer latent period, however, intervenes before their development.

Modifications of the respiratory activity, as well as howls and general agitation, are noted after cutting the vagi, but definite vomiting was never observed by Ducceschi under these conditions.

With but a single intact vagus (the splanchnics being divided) the entire surface of the stomach remains sensitive as indicated by the production of the typical reactions, including vomiting. The degree of sensitivity is, however, considerably less than when both vagi are intact.

The reactions obtained when the splanchnics of one side are alone in connection with the stomach are similar to those noted when both are intact and the sensitivity continues over the entire stomach.

These observations of Ducceschi lead to the conclusion that sensory stimuli are conducted from the stomach by both the vagi and the splanchnics. The stimuli passing by the vagi are, however, alone capable of exciting vomiting. Further, it must be inferred that the vagus and splanchnics of each side have a complete sensory distribution over all parts of the stomach wall. According to Ducceschi, this result is attained, as in the case of the motor innervation, not by the connection of the nerves with Auerbach's plexus but by the very complete anastomoses existing in the oesophageal and coeliac plexuses.

The reaction of vomiting affords an effective means of investigating the sensitivity of a number of the internal organs. Openchowski [6], who studied the action of local emetics in the stomach, concluded that the afferent paths concerned in the production of vomiting by this means are contained in the vagi. He does not, however, furnish any actual experimental details and it is thus impossible to know whether or not he confined the action of the emetic substances strictly to the gastric mucosa, a procedure which appears very desirable in

view of the recent results of a study in man by Hertz, Cook and Schlesinger[7].

A research was, therefore, undertaken by the writer, in the laboratory of Prof. Brodie, with the idea of making a more extensive study of gastric sensation and especially of the paths taken by sensory impulses from the mucous surface of the stomach. An account of the results is given in the Journal of Physiology, vol. XLI, p. 409, 1910.

In selecting a form of stimulation for the gastric mucosa, the faradic current appeared the most desirable. I found, however, that neither the bipolar nor the unipolar method of stimulation, when applied to the mucous surface, was capable of inducing vomiting and, after testing a number of local emetics, I finally resorted to warm mustard solution as yielding the most satisfactory results.

The method of procedure in the experiments with mustard was as follows: — The animal (cat) was anaesthetised with A. C. E. mixture and ether. The abdomen was opened in the middle line and the stomach drawn out and protected by cloths wrung out of warm saline solution. The dorsal and ventral branches of the vagus were then isolated on the oesophagus just below the diaphragm and a ligature tied tightly around the oesophagus underneath the nerves. The pylorus was also firmly ligatured. An opening was made in the ventral surface of the fundus and a glass tube

tied in. The other end of the tube was connected by a piece of rubber tubing with a small funnel. The stomach was emptied and thoroughly washed out. The mustard solution was then introduced. Almost immediately the respirations were increased in rate and force and tongue and swallowing movements, accompanied by salivation, were induced, whilst after an interval of 1—3 minutes, typical vomiting movements ensued. This result may be obtained several times in succession.

It will be seen that under these experimental conditions no actual discharge of the stomach contents is possible and the occurrence of the vomiting reflex is indicated merely by the characteristic contractions of the diaphragm and abdominal muscles. The term vomiting will, accordingly, be employed in this special sense in the remainder of this paper.

In order to determine the afferent paths involved in this vomiting reflex the experiment was carried out as already detailed but, in addition, the splanchnics were isolated on both sides. Vomiting was then excited by mustard. The splanchnics were next divided and it was found that vomiting could still be induced. The vagi were then divided on the œsophagus and it was observed that reflex vomiting was now no longer possible. This has been confirmed in several experiments.

In these experiments the stimulation is limited to the gastric mucosa and we may, therefore, conclude that the vagi alone conduct from this surface the impulses which are capable of exciting vomiting. The splanchnics are, apparently, not in any way concerned in the reflex.

For the purpose of securing tracings of the vomiting movements, the operation on the stomach was performed on a cat anaesthetised with urethane. The respirations were recorded

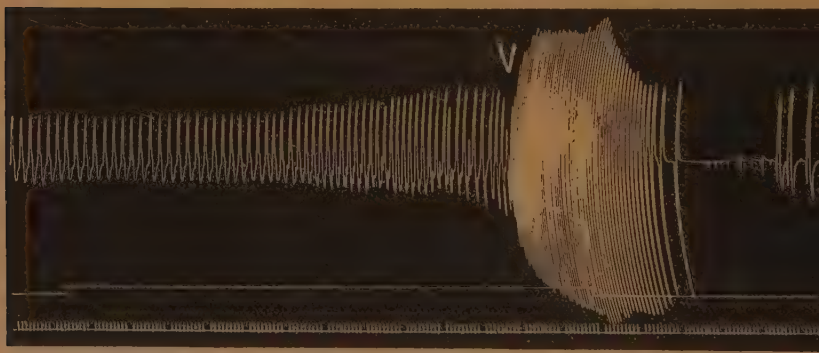

Fig. 1. Record of respirations in cat. Vomiting begins at V. Signal introduction and removal of mustard. Time in seconds.

by causing the animal to breathe into a large bottle connected with a tambour. In fig. 1 is shown the result of introducing a 5 per cent. solution of mustard into the stomach.

The respirations are seen to become considerably quicker and deeper and vomiting occurs in 1 min. 54 secs. The vomiting move-

ments take place with greater frequency than the preceding respirations but become considerably slower after the removal of the mustard from the stomach. Following the vomiting there is a brief interval of rest, after which the breathing is gradually resumed.

With the hope of obtaining further confirmation as to the importance of the vagi in

Fig. 2. Effect of stimulating dorsal vagus. Vomiting occurs at V. Distance of secondary 10 cm. Time in seconds.

reflex vomiting, the effect of electrical stimulation of the vagal branches to the stomach was tested, and it was found possible to excite vomiting by this means.

In fig. 2 is shown the result of exciting the central end of the dorsal vagus with the

faradic current. The respirations, which were recorded in the usual manner, become deeper during the stimulation, and some imperfect attempts at vomiting occur, but complete vomiting does not take place until after the excitation. Powerful vomiting sometimes, however, appears during the actual course of the

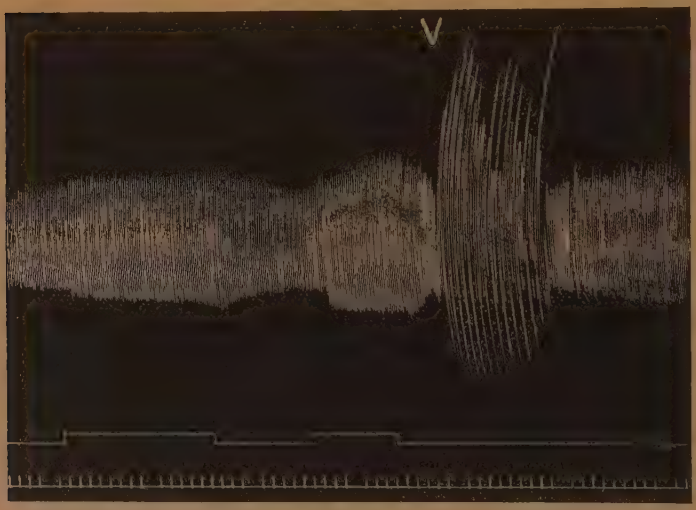

Fig. 3. Effect of stimulating dorsal vagus. Vomiting occurs at V. Distance of secondary 7 cm. Time in seconds.

stimulation. The respiratory excursions are considerably more extensive after, than before, the period of vomiting.

Frequently the nerves must be subjected to several excitations before vomiting is elicited and in these cases a deepening of the respirations is often the only visible evidence

of the stimulation. This is seen in fig. 3 from a later part of the same experiment shown in fig. 2 after the irritability of the nerves has become somewhat reduced.

It was next necessary to ascertain by which vagus trunk in the neck the impulses travel respectively from the dorsal and ventral vagal branches at the lower end of the oesophagus.

In order to determine this point each branch of the vagus was stimulated, whilst the vagi in the neck were successively cooled. The effect of these procedures on the vomiting reflexes was meantime noted. The results indicate that, whilst in some cases, the excitation passes from the dorsal branch exclusively up the right vagus, and from the ventral branch up the left vagus, in many instances impulses from each stomach nerve are transmitted by both vagi.

The final point to be determined in tracing the further course of impulses up the vagi was which of the rootlets belonging to the 9th, 10th and 11th cranial nerves convey the excitation to the medulla. The procedure was as follows. The cat was anaesthetised with A. C. E. mixture and ether and a tracheal tube tied in. The muscles at the back of the neck were then cut through and drawn aside so as to expose the occipital bone and the occipito-atlantal ligament. The dura was carefully separated from the occipital bone by a blunt

hook and the bone cut away, the bleeding being controlled by wax in the usual manner. By these procedures the bone was removed over a considerable area and the underlying dura left intact. A median and two lateral incisions were then made through the dura and the flaps turned out, any bleeding points in the membrane being secured by small clamp-forceps. Under these circumstances it is a simple matter to see the lower medullary rootlets. Vomiting was next induced by stimulating the central ends of the vagal branches to the stomach. The ascending rootlet of the 11th nerve was then divided on each side. Stimulation of the vagus nerves again excited vomiting. The impulses from the stomach causing vomiting are, therefore, not conveyed to the medulla by these rootlets.

In order to expose the upper set of rootlets the preliminary part of the operation was carried out as already described, but in addition a portion of the cerebellum was cut away on the right side and the bleeding stopped by plugging with a piece of cotton wool. The left vagus was previously divided in the neck. Stimulation of the ventral branch of the vagus now caused weak vomiting, whilst stimulation of the dorsal branch caused more powerful vomiting. The upper rootlets on the right side were next divided and it was found that under these circumstances vomiting could no longer be excited by stimulating either gastric nerve.

The difficulties in performing the operation just described are considerable, for the upper rootlets are very deeply situated and, owing to the extensiveness of the procedures required, the animal experiences a great deal of shock. It is hence impossible to cause vomiting by the action of mustard and even stimulation of the gastric nerves frequently proves ineffective.

Accordingly, but a small number of these experiments were successful and the upper rootlets have so far been divided only on the right side. It is reasonable to suppose, however, that thea group of rootlets transmits, on both sides, the afferent impulses which excite vomiting.

As stated earlier, considerable salivation is invariably associated with the vomiting produced by the action of mustard in the stomach and a study was also made of this reflex. For this purpose a cannula was inserted in the submaxillary duct of an animal anaesthetised with chloroform and urethane. Stimulation of the central ends of the vagal branches to the stomach now caused a very definite flow of saliva together with the usual tongue and swallowing movements which precede vomiting. We may, accordingly, infer that the vagi convey impulses from the stomach which are capable of exciting reflex salivary secretion.

The results so far described show the significance of the vagi as afferent gastric nerves

and I now undertook a number of experiments with the object of demonstrating, if possible, whether any similar sensory function night be attributed to the splanchnics.

With this object in view the oesophagus was divided in an animal (cat) anaesthetised with urethane and the pylorus was ligatured. A tube was tied into the opening in the cardia of the stomach and the respirations were recorded in the manner already described. Under these conditions all possible branches of the vagi to the stomach are divided, whilst most, if not all, of the sympathetic connections are retained. It was found, however, that neither the introduction of strong mustard solution nor of bromine water into the stomach caused any alteration in the respiratory movements.

In other experiments a cannula was tied in the submaxillary duct, but mustard solution and bromine water failed to excite any reflex flow of saliva.

I have thus been unable to prove that sensory impulses of any kind are conveyed by the splanchnics from the mucous surface of the stomach and cannot, therefore, add any experimental confirmation to the conclusions of Head.

Literatur.

1. Deutsches Archiv für klinische Medizin. Bd. 30. 1881.
2. Brain, XVI. p. 66. 1893.
3. Virchow's Archiv, XXVI. p. 1. 1863.
4. Archiv für Physiologie, 1864 p. 614.
5. Arch. di Fisiol., p. 521. 1904—1905.
6. Archiv für (Anatomie und) Physiologie, p. 554. 1889.
7. Journ. of Physiol. XXXVII. p. 481. 1908.

Lebenslauf.

Ich bin geboren am 2. Mai 1881 in Toronto, Canada, als Sohn von A. F. Miller. Im Jahre 1899 kam ich auf die Universität Toronto und erhielt 1903 die Würde eines Bachelor of Arts. Von 1903—1905 war ich Assistent der Physiologie an der Cornell-Universität, U. S. A. und führte da meine medizinischen Studien fort. Von 1905—1907 war ich Assistent der Physiologie an der Universität Toronto und 1907 erlangte ich die Würde eines Bachelor of Medicine. Von 1907—1910 war ich Demonstrator der Physiologie an der Universität Toronto und im Jahre 1910 kam ich nach München, um im Physiologischen Institut zu arbeiten.

F. R. MILLER.